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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/341,829	LETHE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,17-22,24,26,29,33,38,43,45,47,49 and 53-61* is/are pending in the application.

4a) Of the above claim(s) *4,5,20-22,24,26,29,33,43,45,47,49,54-56 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,17-19,38,53,57-59 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant election of the species amplification in paper No:17 is acknowledged.

Accordingly, claims 1-3, 6-7, 17-19, 38, 53, and new claims 57-59, 61 are being examined. Claim 60 has been withdrawn from consideration as being drawn to non-elected species.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 is drawn to a unique fragment of nucleotides 1-993 of SEQ ID NO:4 between "15" and 992 nucleotides in length and complements thereof.

The specification does not disclose a unique fragment of nucleotides 1-993 of SEQ ID NO:4 between "15" and 992 nucleotides in length and complements thereof.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

1. Rejection under 35 USC 112, first paragraph of claims 1, 7, 17-19, 38, 53 pertaining to lack of a clear written description of the claimed genus of polynucleotides remains for reasons already of record in paper No.11. New claims 57-59, and 61 are rejected for the same reasons already of record in paper No.11.

Applicant argues that the *Lilly* case does not prohibit definition of a genus of nucleic acid by hybridization to a reference sequence and that the art routinely identifies nucleic acid molecules by hybridization to a particular nucleotide sequence. Applicant argues that hybridization conditions in combination with a reference sequence provide a precise definition of the claimed hybridizing nucleic acid molecules by physical properties. Applicant argues that this sort of identification describes the physical properties of a genus of nucleic acid as surely as IR and MS spectra describe the physical properties of a set of chemical compounds.

Applicant further argues that the claimed molecules must be sufficiently like the reference sequence to hybridize under a specifically defined set of conditions. Applicant argues that since Applicant's invention includes a limited genus of nucleic acid molecules so closely related by physical structure to SEQ ID NO:4 that hybridization under stringent conditions is possible, and since the claimed genus are based on the

description of the genus in the specification, Applicant has fulfilled the requirement for written description.

Applicant argues that one can readily identify whether a particular sequence is part of the claimed genus by performing a simple and well-established hybridization assay.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that unrelated nucleotide sequences sharing with SEQ ID NO:4 a common fragment would hybridize to the claimed SEQ ID NO:4 under stringent conditions. Thus the claims encompass any nucleotide sequence which is structurally unrelated to SEQ ID NO:8, provided said nucleotide sequence shares a fragment with SEQ ID NO:4. Thus, hybridizing to a reference sequence under stringent conditions alone is not sufficient for describing the claimed hybridizing genus; and by hybridization assay, one would obtain unrelated sequences.

Further, concerning nucleic acid sequences comprising fragments of SEQ ID NO:4, the claimed nucleic acid sequences encompass unrelated sequences that share with SEQ ID NO:4 a common fragment.

Concerning unique fragments of SEQ ID NO:4, there is no structural information of the claimed unique fragments. Negative limitation, such as excluding fragments of SEQ ID NO:8 is not sufficient for the description of the structural properties of the claimed unique fragments. Moreover, since the function of SEQ ID NO:4 is not known, the function of the claimed unique fragments is not known either.

Concerning complements of a unique fragment of SEQ ID NO:4, complements could be partial complements wherein partial complements could share with the claimed unique fragment a few nucleotides. Thus the claim 7 encompasses unrelated sequences that share with the claimed unique fragments a few nucleotides.

Thus it is clear that the specification does not describe the necessary common attributes or feature of the elements of the claimed genus. Because the genus is highly variant, the disclosure of SEQ ID NO:4, and nucleic acid molecules that differ from SEQ ID NO:4 in codon sequence due to the degeneracy of the genetic code, is insufficient to decribe the genus. Therefore, only an isolated nucleic acid molecule comprising SEQ ID NO:4, , and nucleic acid molecules that differ from SEQ ID NO:4 in codon sequence due to the degeneracy of the genetic code, but not the full breath of the claims meet the written description provision of 35 USC 112, first paragraph.

2. Rejection under 35 USC 112, first paragraph of claim 6 pertaining to lack of a clear written description of allelic variants of SEQ ID NO:4 remains for reasons already of record in paper No.11.

Applicant asserts that the above arguments for claim 1 are applicable here because claim 6 depends on claim 1.

Applicant argues that Applicant has provided SEQ ID NO:4 and conditions under which a member of the genus are identified, thus Applicant has provided a description against which a potential member of the genus can be compared.

Applicant argues that because of the definition by Reiger et al, that alleles occupy the same chromosomal locus but may differ (slightly) in nucleotide sequence,

and because the chromosomal location of LAGE-1 is provided, one can readily determine if a candidate allele is in fact an allele of LAGE-1 by determining the chromosomal location of the candidate using standard genetic techniques. Applicant asserts that since in most cases, alleles are nearly identical to a reference sequence, a simple comparisons of the sequence of the candidate allele and the reference sequence will generally sufficient to indicate that the candidate allele is an actuall allele. Applicant concludes that chromosomal localization would certainly verify a sequence of very substantially identity as an allele.

Concerning the statement that the genus is highly variant, Applicant argues that this statement does not make sense in the context of a claim for alleles, given that the art recognizes that alleles have substantial identity in nucleotide sequence.

Applicant further asserts that Applicant has set forth the physical properties of the genus that includes alleles of SEQ ID NO:4.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that according to the definition by Reiger et al, allelic variant has one or "more" mutational sites. Thus from the definition by Reiger et al there is no limitation of the number of mutational sites of the allelic variants to "slightly" difference as asserted by Applicant. Further, even in the case of difference in a few nucleotides, there is no teaching whether such allelic variants exist, nor any teaching of where the mutation is in the sequence. Further, since the function of SEQ ID NO:4 is not known, and in view of the fact that function of a nucleotide sequence could be abolished, even

with substitution of only one amino acid of the polypeptide encoded by said nucleotide sequence (Burgess et al, of record), one could not identify the claimed allelic variants by their function.

Further, contrary to Applicant assertion, chromosomal localization is not adequately sensitive to verify a sequence of very substantially identity as an allele. As disclosed the specification, it is suggested that LAGE-1 and MAGE-A gene lie within 2 Mb in the Xq28 band. However, the LAGE-1 signal is superimposed to the MAGE signal (p.44, lines 15-19). Thus using chromosomal localization one would identify unrelated sequences that are at least within the 2Mb regions from the claimed LAGE-1 and are not necessarily an allele of LAGE-1.

The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of allelic variants. The specification and the claims do not place any limit on which nucleotides that are substituted or deleted, or which encoded amino acid subjected to conservative or non-conservative substitution, or deletion, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. In addition, the specification and all other pending claims do not place any limit on the number of amino acids that could be substituted. Thus the scope of the claims includes nucleotide sequences encoding numerous structural variants. The specification and the claims do not provide any guidance as to which, or how many original amino acid(s) are substituted, or to which type of substitution besides conservative substitution, or which amino acids are deleted or inserted so that the encoded polypeptide could function as

contemplated. Structural features, that could distinguish the claimed allelic variant nucleotide sequences from the nucleotide sequences known in the art, are missing from the disclosure. No common structural attributes that identify the claimed allelic variant nucleotide sequences. In addition, no common functional attributes that identify the claimed allelic variant nucleotide sequences are disclosed, because the function of a nucleotide sequence could be abolished, even with substitution of only one amino acid of the polypeptide encoded by said nucleotide sequence (Burgess et al, of record).

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

1. Rejection under 35 USC 112, first paragraph of claim 38 pertaining to lack of enablement for a method for diagnosis of any disorder or cancer using an agent that "selectively binds " to the nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:4, or to a nucleic acid molecule that differs to said hybridizing nucleic acid molecules in codon sequence due to the degeneracy of the genetic code, remains for reasons already of record in paper No.11. New claims 57-59, and 61 are rejected for the same reasons already of record in paper No.11.

Applicant argues that selective binding is recognized term used in patent claims to indicate that the binding between two binding partner is specific. The claims as filed embraced binding interactions of different types, e.g. hybridization between nucleic acids and antigen-antibody binding.

Applicant further argues that it is routine experimentation as nucleic acid hybridization is well known in the art. Applicant has provided guidance in the form of

specific hybridization conditions, as well as working examples pertaining to hybridization and nucleic acid amplification of SEQ ID NO:4.

Applicant further request a scientific reference that set forth a principle that under low stringent hybridization conditions, any compound would bind to the claimed nucleic acid molecules.

Concerning probes that are specific for SEQ ID NO:4, Applicant asserts that Figure 1 shows a region of SEQ ID NO:4 that is absent from SEQ ID NO:6 and SEQ ID NO:8 or NY-ESO-1, and that this region would be adequate to distinguish the expression of SEQ ID NO:4 from other related sequences. Applicant further asserts that even if primers that bind to all three sequences were used in PCR amplification reaction, the sizes of amplification products are different among these three sequences, and thus are distinguishable by one of ordinary skill in the art.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the claims are drawn to an agent that "selectively binds" to a nucleic acid molecule and not an antibody that selectively binds to an antigen. Further, since there is no definition in the specification of "selectively binds", the claims encompass a method for detecting a disorder characterized by expression of LAGE-1 nucleic acid molecule, using an agent that binds to SEQ ID NO:4 under any degree of selectivity, from very low to very high selectivity, or any hybridization conditions. Thus clearly, one would expect that the claimed agent that binds to SEQ ID NO:4 under very low selectivity would also bind to unrelated nucleic acid sequences of the test samples.

Moreover, it is notoriously well known in the art that under very low stringent hybridization conditions, non-specific binding by mismatch hybrids and non-sequence specific interactions occur (Ausubel, FM et al, eds, 1987, Current protocols in molecular biology, John Wiley & Sons, New York, pages 6.3.5). Thus given the broadest interpretation, the claimed method would not detect any disease.

Moreover, the claims also encompass a method for detecting a disorder characterized by expression of LAGE-1 nucleic acid molecule, using primers that are specific for SEQ ID NO:4. There is however no teaching in the specification which primers are specific for SEQ ID NO:4, nor there is any indication that there are primers that are specific for SEQ ID NO:4, in view of the fact that there is high homology among SEQ ID Nos: 4, 6 and 8, and in view of the fact that Applicant has not shown that the small region of SEQ ID NO:4 that is absent from SEQ ID NO:6 and SEQ ID NO:8 or NY-ESO-1 is different from all other sequences that are known in the art.

Concerning the argument that even if primers that bind to all three sequences were used in PCR amplification reaction, the sizes of amplification products are different among these three sequences, and thus are distinguishable by one of ordinary skill in the art, detection of the size of the amplified sequences is not recited in the claims. Thus Applicant argues limitation that is not in the claims.

2. Rejection under 35 USC 112, first paragraph of claim 53 pertaining to lack of enablement for a vaccine composition comprising the nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:4, or to a nucleic acid molecule that differs from said hybridizing nucleic acid molecules in codon sequence due to the

degeneracy of the genetic code, or complete complements thereof, remains for reasons already of record in paper No.11.

Applicant argues that concerning Ezzell et al, the unsettled nature of an effective approach to immunization hardly has a bearing on whether one of ordinary skill in the art would have to exercise undue experimentation to make and/or use the claimed approach. Applicant asserts that four examples are included in the response, showing that the scientific literature contains many examples of the use of nucleic acid immunization to generate immune responses.

Applicant further asserts that one needs not provide information that permits one of ordinary skill to predict the efficacy of a therapeutic invention in order to enable the invention.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the four recited examples are not included in the response and could not be considered.

Although there might be some successful cancer treatment using nucleic acid immunization, the art overwhelmingly teaches that cancer treatment is unpredictable (Ezzell et al, Spitler et al, and Boon et al, all of record). Thus based only on an example of the presence of SEQ ID NO:4 in some cancers, one could not extrapolate that SEQ ID NO:4 could be used for cancer treatment, in view of the unpredictability of cancer treatment.

In addition, MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling." There is overwhelming evidence in the art that treatment of cancer is unpredictable, as taught by Ezzell et al, Spitler et al, and Boon et al (all of record).. However, the specification lacks guidance on necessary dosages and treatment schedules for successful use of the claimed SEQ ID NO:4 in the treatment of cancer *in vivo*.

3. Rejection under 35 USC 112, first paragraph of claims 1, 38 and 53 pertaining to lack of enablement for a nucleic acid molecule that differs from the nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:4 in "codon sequence" due to the degeneracy of the genetic code, and a nucleic acid molecule "encoding LAGE-1", remains for reasons already of record in paper No.11. New claims 57-59, and 61 are rejected for the same reasons already of record in paper No.11.

Applicant argues that determination of protein expression is routine in the art. Applicant further argues that the proteins encoded by the nucleic acids in the references are in fact translated, although not necessarily in proportion to the amount of mRNA produced. Applicant asserts that even if pecularity like those cited in the references were to apply, and there is no indication that this is so, one would not have to engage in undue experimentation to determine if LAGE-1 protein is translated.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is clear from the reference by Fu et al that p53 protein in some cases is not detected (see figure 3). Further, this is not a pecularity, as also shown by Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475), who teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Moreover, it is well known in the art that regulation of mRNA translation is one of the major regulatory steps in the control of gene expression (Jansen, M et al, 1995, Pediatric Res, 37 (6): 681-686). Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. In addition, although determination of protein expression is routine in the art, however, since it is unpredictable whether the encoded LAGE-1 protein exists in nature,

it would have been undue experimentation for one of skill in the art to practice the claimed invention.

4. Rejection under 35 USC 112, first paragraph of claims 3, 17-19 pertaining to lack of enablement for a nucleic acid molecule comprising a "coding region" of SEQ ID NO:4, remains for reasons already of record in paper No.11.

The arguments and answers in the above item # 3 apply here as well.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Rejection under 35 USC 112, first paragraph of claims, 1, 7, 17-19, 38 and 53 pertaining to lack of enablement for nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:4, or complements of unique fragments of SEQ ID NO:4, remains for reasons already of record in paper No.11. New claims 57-59, and 61 are rejected for the same reasons already of record in paper No.11.

Applicant argues that the Examiner does not provide any reasons why a substantial number of molecules encompassed by the claims would be expected not to share the properties of SEQ ID NO:4. Applicant asserts that the claimed invention requires that the claimed nucleic acid molecules share structural properties (sequence hybridization) and functional properties with SEQ ID NO:4.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that unrelated nucleotide sequences sharing with SEQ ID NO:4 a common fragment would hybridize to the claimed SEQ ID NO:4 under stringent

conditions. Thus the claims encompass any nucleotide sequence which is structurally unrelated to SEQ ID NO:8, provided said nucleotide sequence shares a fragment with SEQ ID NO:4. Further, the function of the claimed sequences are not known, because the specification does not disclose the function of SEQ ID NO:4 to which the claimed sequences hybridize under stringent conditions.

Concerning complements of a unique fragment of SEQ ID NO:4, complements could be partial complements wherein partial complements could share with the claimed unique fragment a few nucleotides. Thus the claim 7 encompasses unrelated sequences that share with the claimed unique fragments a few nucleotides.

2. Rejection under 35 USC 112, first paragraph of claims 1, 6 pertaining to lack of enablement for allelic variants of SEQ ID NO:4, remains for reasons already of record in paper No.11.

Applicant argues that the claims recite nucleic acid molecules, and that the Examiner however set forth some of the unpredictabilities of protein chemistry. Thus this is an irrelevant and insufficient basis for making an enablement rejection.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the Office recited that such unpredictability of protein chemistry would equally apply to DNA sequences which encode proteins (p.18, last paragraph).

3. Rejection under 35 USC 112, first paragraph of claim 38 pertaining to lack of enablement for a method for detecting a disorder characterized by expression of SEQ

ID NO:4, remains for reasons already of record in paper No.11. New claims 57-59 are rejected for the same reasons already of record in paper No.11.

Applicant argues that the law does not require that Applicant provides a recitation of each and every disorder in which LAGE-1 is overexpressed to enable the diagnostic method. Applicant argues that future work by others may identify diseases other than cancers that have LAGE-1 overexpression and that the role of SEQ ID NO:4 in other diseases is not equired to be known in order to practice the claimed method based on detection of expression.

Applicant further argues that the claimed invention is not a method for identification of disorders that have LAGE-1 overexpression. The claimed invention merely recites the use of LAGE-1 nucleic acid molecules in the diagnosis of disorders. This invention stems from the identification of the expression pattern of LAGE-1, and in view of this expression pattern, one is enabled to diagnose disorders based on the expression of LAGE-1.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

As written, the claims encompass a method for identification of any disorder that has LAGE-1 overexpression.

Although LAGE-1 is overexpressed in various cancers, one cannot predict that LAGE-1 is overexpressed in any other disease, because different diseases have different characteristics and etiology.

Further, one cannot extrapolate from a single example of overexpression of LAGE-1 in cancers to overexpression of LAGE-1 in any other disease. MPEP 2164.08(a) teaches that a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claims because the specification disclosed at most only those means known to the inventor. *In re Hyatt*, 708 F.2d 712, 714-715, 218 USPQ 195, 197 (Fed. Cir. 1983). In the instant application, the specification only discloses that SEQ ID NO:4 is overexpressed in cancers, however, the scope of the claims encompass overexpression of LAGE-1 in any disease, wherein LAGE-1 is used for detection of any disease. Thus the claims would be non-enabled according to MPEP 2164.08(a).

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT, NEW REJECTION

Claims 58-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 58-59 are drawn to a method for diagnosing a disorder characterized by expression of LAGE-1 nucleic acid molecule, by nucleic acid amplication or PCR, using "an" agent that selectively binds to nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:4, or to a nucleic acid molecule that differs to said hybridizing

nucleic acid molecules in codon sequence due to the degeneracy of the genetic code, or to complete complements thereof.

Claims 58-59 encompass a method for diagnosing a disorder characterized by expression of LAGE-1 nucleic acid molecule, by nucleic acid amplication or PCR, using a single primer that selectively binds to nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:4, or to a nucleic acid molecule that differs to said hybridizing nucleic acid molecules in codon sequence due to the degeneracy of the genetic code, or to complete complements thereof.

It is not clear how one could perform PCR using a single primer. It is well known in the art that two primers are required for PCR (Sambrook et al, eds, 1989, Molecular cloning, a Laboratory manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, p. 14.2-14.4).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

November 18, 2002